

Methods of Optimizing Antibody
Variable Region Binding Affinity

BACKGROUND OF THE INVENTION

This invention relates generally to a method of
5 monoclonal antibody production and specifically to the
simultaneous *in vitro* affinity optimization of multiple
distinct domains of a variable region of a monoclonal
antibody.

The War on Cancer is entering its third decade
10 and recent years have shown tremendous progress in the
understanding of cancer development and progression yet
there has been only marginal decreases in death rates
from most types of cancer. Standard chemotherapy and
radiation therapy generally involve treatment with
15 therapeutic agents that impact not only cancer cells but
other highly proliferative cells of the body, often
leading to debilitating side effects. Thus, it is
desirable to identify therapeutic agents with a higher
degree of specificity for the carcinogenic lesion.

20 The discovery of monoclonal antibodies (mAbs)
in the 1970's provided great hope for the reality of
creating therapeutic molecules with high specificity.
Antibodies that bind to tumor antigens would provide
specific targeting agents for cancer therapy. However,
25 while the development of monoclonal antibodies has
provided a valuable diagnostic reagent, certain
limitations restrict their use as therapeutic entities.

A limitation encountered when attempts are made
to use mAbs as therapeutic agents is that since mAbs are

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PATENT

Our Docket: P-IX 3458

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Huse et al.

Serial No.: 09/434,870

Filed: November 4, 1999

For: METHODS OF OPTIMIZING
ANTIBODY VARIABLE REGION
BINDING AFFINITY

Group Art Unit: 1643

Examiner: Not Yet Known

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C., 20231 on October 10, 2000.

Commissioner for Patents
Washington, D.C. 20231

By: David A. Gay
David A. Gay, Reg. No. 39,200

October 10, 2000
Date of Signature

Sir:

PRELIMINARY AMENDMENT

Prior to Examination of the above-identified application, entry of the following amendment is respectfully requested.

IN THE SPECIFICATION:

On page 1, before the first paragraph, please insert the paragraph:

--This application claims the benefit of priority of provisional application Serial No. 60/159,689, filed October 14, 1999, which is incorporated herein by reference.--

On page 8, line 10, please substitute the phrase "Chothia et al." with the phrase --Chothia and Lesk--